REMARKS

Applicants submit this paper is submitted in response to the final office action the Office mailed on December 8, 2005.

Nonstatutory double patenting

The Office provisionally rejected claims 50-56, 58, 60-74 and 76-79 under judicially created obviousness-type double patenting over claims 1-4 and 9-11 of copending application No. 10/651,515. Applicants respectfully traverse the rejection and note that this rejection is not procedurally ripe for consideration. Because of this, Applicants request the Office to hold this provisional rejection in abeyance until patentable subject matter is identified in either or both of these applications. The filing of a terminal disclaimer at this time is premature. Once patentable subject matter is identified, Applicant can properly address this issue, the terms of which will depend on the scope of allowable subject matter in these applications.

35 U.S.C. § 112, first paragraph

The office rejected claims 50-56, 58, 60-74 and 76-79 as allegedly not enabled for preventing innate immune deficiency due to radiation exposure. The office rejected claims 50-56, 58 and 60-66 as allegedly not enabled because the specification lacked written description to support claim limitations of "about 4-40 mg/kg/day" and "7 consecutive days" at claim 65. Applicants respectfully traverse both rejections.

To establish and maintain a rejection under 35 U.S.C. §112, first paragraph, the Office must provide logical reasoning to support its position. The Office must "explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." *In re Marzocchi and Horton*, 169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971). The Office must advance "substantive reasons why the instant specification is non-enabling." "Mere broad generalizations and allegations are insufficient for holding of non-enablement." *Ex parte Goeddel* 5 U.S.P.Q. 2d 1449 (B.P.A.I. 1987). The

first paragraph of 35 U.S.C. § 112 requires nothing more than objective enablement. *In Re Vaeck* 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991), *Atlas Powder Co. v. E.I. Du Pont De Nemours & Co.* 224 U.S.P.Q. 409 (Fed. Cir. 1984). It is irrelevant whether objective enablement is based on working examples or on broad terminology. *In Re Vaeck*, supra, *Atlas Powder Co.*, supra. To meet the requirement under the first paragraph of § 112, the specification, when filed, must enable one skilled in the particular art to use the invention without undue experimentation. *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988), *Ex parte Forman* 230 U.S.P.Q. 546 (B.P.A.I. 1986). In addition, even if some of the claimed embodiments were inoperative, the claims are not necessarily invalid. "It is not a function of the claims to specifically exclude . . . possible inoperative substances . . . ." *Atlas Powder Co.*, supra, *In re Dinh-Nguyen*, 492 F.2d 856 (C.C.P.A. 1974).

The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art. *In re Wands, supra*. The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. *Ex parte Jackson, et al.*, 217 U.S.P.Q. 804 (B. P. A. I. 1982), *In re Ranier, et al.*, 146 U.S.P.Q. 218 (C.C.P.A. 1965). As explained below, Applicants respectfully submit that the claimed subject matter is enabled.

In casting the first rejection, the office alleged that (1) there were no known methods to prevent innate immune suppression due to radiation, (2) the specification lacks guidance or working examples of preventing innate immune suppression due to radiation and (3) the skilled artisan would have to search the prior art to find a model for "determining a person prone to innate immune suppression" and therefore needing treatment.

The specification contains guidance and a working example showing that the methods and compounds can prevent the development of innate immune

suppression. Example 3 at paragraphs 623-627 (specification pages 213-215) describe treatment of non-human primates that were infected with an aggressive retrovirus, $SHIV_{229}$, which is a recombinant retrovirus containing HIV and SIV sequences. As example 3 describes, the animals' specific or adaptive immunity was profoundly suppressed as shown by low $CD4^+$ cell counts in the animals. All of the treated animals were not only were kept alive for over 350 days by the monotherapy, they appeared to be clinically healthy and without opportunistic infections or other clinically significant disease-related symptoms. The clinical health of the animals was achieved, despite the existence of an otherwise lethal specific immune suppression condition. As described at paragraph 626, the mean time to death of untreated animals was 193 days. Since the treated animals did not die from SHIV-induced specific immunity suppression, their survival depended on sustained innate immunity. The treated animals did not have a clinically apparent innate immune suppression condition; otherwise they would have succumbed to infection. Applicants respectfully submit that the specification discloses a working example that shows prevention of an innate immune suppression condition after treatment in a subject prone to develop such a condition.

A second example of preventing innate immune suppression is disclosed in Dowding et al, *Blood* 102(11 part 2):44b, abstract# 3878 2003 (of record). The previously cited Dowding et al reference shows that androst-5-ene-3β,17β-diol completely prevented grade 3 neutropenia in macaque monkeys caused by carboplatin chemotherapy, while four out of five placebo treated control animals developed grade 3 neutropenia. Example 3 discussed above shows how to prevent innate immune suppression in the context of a chronic viral infection. Dowding et al shows how to prevent innate immune suppression in the context of an immune suppressive chemotherapy. There is no reason to believe that the same treatment methods could not be used to prevent innate immune suppression from a radiation exposure. The office provided no rationale as to why, in view of example 3 and the Dowding et al reference, the same treatment

methods could not be used to prevent innate immune suppression due to a radiation exposure. Applicants submit that is evidence cannot just be ignored.

All of the details of how one would prevent innate immune suppression are explicitly and clearly taught in the specification. The teaching includes dosing regimens and daily doses that were used to prevent innate immune suppression, see, e.g., example 3 (paragraph 623), short term daily dosing (paragraph 222), hypothetical human dosing example disclosing 1 to 10 mg/kg/day doses for 4 to 10 days (paragraph 355) and dosing of about 0.1-10 mg/kg/day, administered parenterally (paragraph 599). The specification satisfies the enablement requirement for the claimed subject matter. *In Re Vaeck*, supra, *Atlas Powder Co.*, supra.

The office alleged that the skilled artisan would have to search the prior art to find a model for "determining a person prone to innate immune suppression" and therefore needing treatment. Applicants respectfully traverse this allegation. First, the claims recite therapeutic treatment methods and it is reasonable to posit that one of ordinary skill in the art is a health care provider. Competent health care providers are familiar with situations or clinical conditions that can or will lead to innate immune suppression and there is therefore no need to look for a model to determine who may require treatment. Second, the specification itself specifies clinical conditions or situations that lead to immune suppression, e.g., chemotherapy or radiation exposure, pathogen infection or cancer (at, e.g., paragraphs 457, 519, 521 and 597). In casting the rejection, the office did not explain why a model to determine who would need treatment was necessary for one of ordinary skill in the art to know when the treatment method should be used. Nor did the office explain why the disclosure in the specification was insufficient. Absent a rationale showing that some type of model is necessary despite Applicant's express teaching, the office's allegation is a mere broad generalization, that is based at least in part on the office's incorrect allegation that the specification lacks a working example. *Ex parte Goeddel*, supra. Applicants request reconsideration and withdrawal of the rejection.

The office rejected claims 50-56, 58 and 60-66 as allegedly not enabled because the specification lacked written description to support claim limitations of "about 4-40 mg/kg/day" and "7 consecutive days" at claim 65. Support for dosing about 4-40 mg/kg/day is at paragraph 218. Support for 7 days of dosing is at paragraph 592. Applicants are unsure of why the office alleged that these disclosures were not present because Applicants identified these paragraphs for the office in their prior response. Applicants request reconsideration and withdrawal of the rejection.

35 U.S.C. § 103(a)

The Office rejected claims 50-56, 58, 60-74 and 76-79 as allegedly unpatentable over U.S. patent No. 5,461,042 (hereafter '042, of record). Applicants respectfully traverse the rejection.

Obviousness rests on several factual underpinnings: (1) the scope and content of the prior art, (2) the differences between the prior art and the claimed invention, (3) the level of skill in the art, and (4) the objective indicia of nonobviousness. *Panduit Corp. v. Dennison Mfg. Co.*, 810 F.2d 1561, 1566-67, 1 U.S.P.Q.2D (BNA) 1593, 1595-96 (Fed. Cir. 1987); *Graham v. John Deere Co.*, 383 U.S. 1, 17, 15 L. Ed. 2d 545, 86 S. Ct. 684 (1966). To establish a case of prima facie obviousness under § 103, consideration of whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991), *In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988). Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure. *Velander v. Garner*, 348 F.3d 1359; 2003 US App LEXIS 227172003 U.S. App. LEXIS 22717; 68 USPQ2D (BNA) 176968 U.S.P.Q.2D (BNA) 1769 (Fed. Cir. 2003). In establishing obviousness, the determination must involve more than indiscriminately combining prior art. *Micro Chem., Inc. v. Great Plains Chem. Co.*, 103 F.3d 1538,

1546 (Fed. Cir. 1997). To avoid impermissible hindsight-based obviousness analysis, one must rigorously apply the requirement for a showing of a teaching or motivation to combine prior art references. *Ecolochem, Inc. v. Southern Cal. Edison Co.*, 227 F.3d 1361, 1372 (Fed. Cir. 2000) (citing *In re Dembiczak*, 175 F.3d 994, 999 (Fed. Cir. 1999), abrogated on other grounds by *In re Gartside*, 203 F.3d 1305 (Fed. Cir. 2000)). To avoid the subtle but powerful attraction of a hindsight-based obviousness analysis, it is necessary to rigorously apply the requirement for a showing that the teaching or motivation to combine prior art references is in those references and not in the patent applicant's own disclosure. *In re Dembiczak, supra*.

As Applicants stated in their prior response, the '042 patent does not disclose any daily dosing regimen and it does not disclose any mg/kg/day dosage, either or both of which are presently claimed. Because of this, the office has not established a prima facie case of obviousness for any claim and the rejection is improper and clearly based on impermissible hindsight. *In re Dembiczak, supra*. The office's reliance on *In re Russell*, 439 F.2d 1228 (CCPA 1971) is misplaced because that case does not change the office's burden to establish the prima facie case. *In re Russell* dealt with changes of ranges that were known in the prior art. The '042 patent discloses none of the claimed ranges and it cannot render the claims obvious or unpatentable. In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection.

Concluding remarks

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 501536.

Respectfully submitted,

Hollis-Eden Pharmaceuticals, Inc.

Date: February 8, 2006 By: Daryl D Muenchau

Daryl D. Muenchau, Reg. No. 36,616
Hollis-Eden Pharmaceuticals, Inc.
4435 Eastgate Mall, Suite 400
San Diego, CA 92121
Phone: 858-320-2569
Fax: 858-558-6470